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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,118	10/15/2003	Paul R. Hinton	05882.0039.NPUS04	7362

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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 12/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,118	HINTON ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,15-28,31-43,49,52-65 and 67-69* is/are pending in the application.

4a) Of the above claim(s) *4,7,15-17,22,31-33,54-65 and 67-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 6, 8-12, 18-21, 23-28, 34-43, 49, 52, and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures, except for the following.

2. Applicant's election without traverse of Group I and the species 0f OST577 IgG2 antibody and amino acid positions 250 and 428, filed 10/24/05, is acknowledged.

Claims 1-12, 15-28, 31-43, 49, 52-65 and 67-69 are pending.

Claims 4, 7, 15-17, 22, 31-33, 54-65, and 67-69 have been withdrawn from consideration by the Examiner, under 37 C.F.R. 1.142(b), as being drawn to nonelected inventions.

Claims 1-3, 5, 6, 8-12, 18-21, 23-28, 34-43, 49, 52, and 53, drawn to a modified antibody or antibody fragment of IgG that read on the elected species of OST577 IgG2 and amino acid residues altered at positions 250 and 428, are under consideration.

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The priority applications upon which benefit is claimed appears to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

4. The application is required to be reviewed and all spelling, TRADEMARK, and like error corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent application, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

5. Applicant's IDSs, filed 10/29/2004, 03/10/2005, and 06/07/2005, are acknowledged. Applicant's submission of Search Report on the IDS filed 09/07/05 is acknowledged, however, this citation has been crossed out as it is not appropriate for printing on an issued US Patent.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-3, 5, 6, 8-12, 18-21, 23-28, 34-43, 49, 52, and 53, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-3, 5, 6, 8-12, 18-21, 23-28, 34-43, 49, 52, and 53 are indefinite in that they only describe the number of amino acid residue positions without reciting the numbering system.

It is suggested to amend the claim to recite the particular numbering system used (e.g. EU numbering system).

B) Claim 6 is indefinite in the recitation of "OST577-IgG2M3" and "OST577-IgG1" because their characteristics are not known. The use of "OST577-IgG2M3" and "OST577-IgG1" as the sole means of identifying the claimed antibodies redden the claim indefinite because "OST577-IgG2M3" and "OST577-IgG1" are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same designations to define completely distinct biological materials.

Amending the claim to recite the appropriate Deposit Accession Number or SEQ ID NOs would obviate this rejection. See the rejection under the first paragraph of 35 U.S.C. 112 for the deposit of biological materials below.

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As required elements, the antibodies "OST577-IgG2M3" and "OST577-IgG1" must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell lines/hybridomas which produce "OST577-IgG2M3" and "OST577-IgG1". See 37 CFR 1.1801-1.1809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in US patent applications.

Amendment of the specification to recite the date of the deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified. See MPEP 1.804(b).

Further it is noted that the sequence of an entire immunoglobulin satisfies the enablement requirements under 35 USC 112, first paragraph as well.

Note that satisfaction for the enablement of biological materials such as the claimed "OST577-IgG2M3" and "OST577-IgG1" requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 8-12, 18, 19, 24-28, 34-43, 49, 52, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al. (Molecular Cell, 2001, 7:867-877) (see entire document) as evidenced by Hinton et al. (JBC, 2004, 279;(8):6213-6216) (see entire document).

Martin et al. teach mechanism of pH-dependent binding between the neonatal Fc receptor (FcRn) and IgG Fc (see entire document, especially the Title and Abstract). Specifically, Martin et al. predict that most of the mutations in the Fc region that would enhance IgG Fc binding to FcRn reside near the region predicted to contact FcRn (e.g. see Figure 3 on page 874) including position 250 (e.g. see page 874, right column) and 428 (e.g. see page 875, left column). Further, Martin et al. teach that mutagenesis protocol allowing all possible non-glycine, non-proline amino acid residue substitutions at above mentions positions would enhance the binding affinity of IgG Fc to FcRn. Furthermore, Martin et al. teach that understanding the mechanism of pH-dependent IgG Fc-FcRn interaction will benefit efforts to design therapeutic antibodies with longer serum half-lives (e.g. see page 875, left column).

As is evidenced by Hinton et al., IgG mutants T250Q and M428L show increased binding to FcRn at pH 6.0 and no binding at pH 7.5 (see entire document, particularly page 6215, left column) and with an in vivo mean serum clearance rate about 1.8-1.9 fold lower than that of the corresponding unmodified antibody (e.g. see page 6216, left column).

Given the referenced teachings that IgG Fc mutated at position including 250 and 428 would have increased binding affinity to FcRn and longer serum half-life; the claimed functional limitations of in vivo mean serum clearance rate and pH-dependent binding would be inherent properties of the referenced teachings.

Therefore, the reference teachings anticipate the claimed invention.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 2, 3, 5, 6, 20, 21, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martin et al. (Molecular Cell, 2001, 7:867-877) (see entire document) in view of Reff et al. (Critical Review in Oncology/Hematology, 2001, 40:25-35) and Ogata et al (PNAS, 1993, 90:3014-3018).

The teachings of Martin et al. have been discussed, supra.

The teachings of Martin et al. differ from the instant claims by not describing human antibody of IgG class and OST577 antibody.

Reff et al. teach that in order to make antibodies better tolerated in humans, techniques such as transgenic mice are developed where the murine Ig genes have been replaced with human IgG genes, are developed to produce human antibodies (see entire document, particularly page 27).

Ogata et al. teach that a human monoclonal antibody directed against the α determinant of HBV surface antigen delayed infection of HBV and hepatitis in the chimpanzee (see entire document, particularly the Abstract and Results on pages 3015-3016).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce human IgG for better tolerance taught by Reff et al. and to make OST577 antibody for potential therapeutic advantage against HBV infection taught by Ogata et al. and enhance their binding to FcRn by substituting amino acid at positions 250 and 428 of the Fc region for prolonged serum half-lives taught by Martin et al.

One of ordinary skill in the art would have been motivated to do so because Martin et al. teach that mutations at Fc region including positions 250 and 428 of an antibody would enhance its binding to FcRn resulting in prolonged serum half-life; and Reff et al. teach method of making human antibody that is better tolerated in treating human patients and Ogata et al. teach OST577 antibody delays HBV infection and hepatitis in experimental animal.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-3, 5, 8-10, 12, 19-21, 23-28, 34-43, 49, 50, and 53 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 13 and 15 of copending USSN: 10/822,300.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant and copending claims are drawn to same or nearly the same modified antibodies with the same modifications to the heavy chain constant regions for enhancing FcRn binding affinity and/or increasing serum half-life.

Further, although the '300 copending Application recites antibodies daclizumab, fontolizumab, visilizumab and M200, they were well known in the art at the time the invention was made. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prolong the serum half-lives of the therapeutic antibodies by mutating amino acids at Fc region to enhance binding to FcRn. The ordinary artisan would have been motivated to do so because mutations at Fc region of an antibody can enhance its binding to FcRn therefore prolong serum half-life.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 1-3, 5, 8-10, 12, 18-21, 23-28, 34-43, 49, 50, and 53 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 7-13, 15, 17-19 of copending USSN: 10/966,673.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant and copending claims are drawn to same or nearly the same modified therapeutic proteins with the same modifications to the heavy chain constant regions for enhancing FcRn binding affinity and/or increasing serum half-life.

Further, although the '673 copending Application recites a modified Fc-fusion protein or antibody fragment; it is well known in the art at the time the invention was made that mutations in Fc region that enhanced binding to FcRn would be beneficial in increase serum half-life for therapeutic proteins (e.g. antibodies, fusion proteins); therefore it would have been obvious to one of ordinary skilled in the art at the time the invention was made to combine therapeutic protein with Fc region of IgG to enhance protein serum half-life. The ordinary artisan would have been motivated to prolong the serum half-lives of therapeutic proteins by fusing it to an Fc region that further carries amino acid mutations to enhance binding to FcRn and to increase serum half-life of the therapeutic protein of intent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 1-3, 5, 8-10, 12, 18-21, 23-28, 34-43, 49, 50, and 53 directed to an invention not patentably distinct from claims 1-5, 7-13, 15, 17-19 of commonly assigned USSN: 10/966,673 for the reasons stated above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned USSN: 10/966,673, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
December 9, 2005

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12/11/05